REMARKS

Reconsideration of this application is respectfully requested.

Claims 37-42 have been canceled. Applicants reserve the right to prosecute the subject matter of the canceled claims in a related application.

Claims 43-61 have been added to the application. These claims are supported in the application as follows.

Claims 43 and 49 are derived from claim 37 and the disclosure at page 5, lines 6-12 of the specification.

Claims 44 and 50 are supported at page 5, lines 11-12 of the specification.

Claims 45, 46, 51, and 52 are based on the disclosure at page 7, lines 19-26.

Claims 47 and 53 are based on the disclosure at page 9, lines 5-8.

Claims 48 and 54 are supported by the disclosure at page 9, lines 9-14 of the application.

Claim 55 is supported at page 8, lines 20-24 of the application.

Claim 56 is supported at page 7, lines 23-26 and page 8, lines 25-26 of the specification.

Claims 57-61 are based on canceled claims 39-42, respectively.

Applicants' invention relates to a method for the *in vitro* detection of an infection due to *H. pylori* in a sample of biological fluid from a patient, wherein the method comprises: a) bringing the sample into contact with an *H. pylori* bacterial strain (claims 43-48), or a bacterial extract from an *H. pylori* bacterial strain (claims 49-61) having an aflagellate phenotype resulting from a mutation in the *flbA* gene of said *H. pylori*

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bacterial strain such that either the *flbA* gene is no longer expressed in the *H. pylori* bacterial strain, or the expression of the *flbA* gene in the *H. pylori* bacterial strain does not enable the A and B flagellins or the sheath that contains them to be biosynthesized and, if this is the case does not enable the *H. pylori* anchoring protein or the hook to be synthesized; and b) detecting an immunological reaction between the bacterial strain and antibodies directed against *H. pylori* and which are present in the sample.

Claims 37-38 were rejected under 35 U.S.C. §112, second paragraph, as allegedly being indefinite for failing to particularly point out and distinctly claim the subject matter that applicants regard as their invention. The Office stated that several phrases in the claims were deemed to be indefinite, including "or of a nucleotide sequence of a *flbA* gene", "which has been amplified using two", "are able to hybridize, under conditions of high stringency, with these nucleotides", and "these nucleotides". This ground for rejection has been obviated by the cancellation of claims 37-38. The quoted expressions, which the Office found to be objectionable, do not appear in the new claims.

Applicants respectfully traverse the rejection to the extent that it is based on use of the word "or" in a list of alternative embodiments. For example, the word "or" appears in new claims 47 and 53. Use of the term "or" in the context of alternative embodiments is conventional in U.S. practice, and there is no apparent reason why it should be found to be objectionable.

Finally, the Office indicated that the claimed method "should clearly delineate the steps involved in the method and the limitations of the various reagents." (Paper No. 11

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at 4, lines 10-11). This requirement has been met. The new claims clearly delineate the steps involved in the method and also recite the essential reagents.

Claim 42 was rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter that applicants regard as their invention. This rejection has be obviated by the cancellation of claim 42. While claim 60 is derived from claim 42, claim 60 uses different language, not the language the Office found to be objectionable in claim 42. Accordingly, the rejection under 35 U.S.C. §112, second paragraph, should be withdrawn.

Claims 37-39 and 40-42 were rejected under 35 U.S.C. §102(b) as being anticipated by Haas et al., Mol. Microbiol., 1993, 8(4):753-60. This ground for rejection is respectfully traversed and reconsideration is requested for the following reasons.

Applicants' claims recite a method for the *in vitro* detection of an infection due to *H. pylori* in a sample of biological fluid from a patient. The method comprises bringing the sample into contact with an *H. pylori* bacterial strain or an extract thereof having an aflagellate phenotype resulting from a mutation in the *flbA* gene. Either the *flbA* gene is no longer expressed in the *H. pylori* bacterial strain, or the expression of the *flbA* gene in the *H. pylori* bacterial strain does not enable the A and B flagellins or the sheath that contains them to be biosynthesized and, if this is the case does not enable the *H. pylori* anchoring protein or the hook to be synthesized.

The Office asserted that in the Haas et al. reference, the rabbit used to make antibodies is a "patient", and the "patient's" antisera was a biological fluid. Applicants courteously submit that this contention is not sustainable. The Haas et al. reference

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does not contain any description of an infection due to *H. pylori*. The rabbit used to make the antibodies disclosed in Haas et al. (AK183 and AK178) was never infected with *H. pylori*. Rather, the rabbit received injections of an FlaA fusion protein, in the case of AK183, or of a purified mixture of FlaA and FlaB proteins, in the case of AK178.

Moreover, in the Haas et al. reference, the aflagellate phenotype results from a mutation in an *flaA* gene. This gene is clearly distinct from the "*flbA*" gene recited in applicants' claims. Accordingly, the Haas et al. reference can not anticipate claims 43-61 because the reference does not disclose all of the features of these claims. The rejection of applicants' claims under 35 U.S.C. §102(b) as being anticipated by Haas et al. should be withdrawn.

Claims 37-39 were rejected under 35 U.S.C. §102(b) as being anticipated by O'Toole et al., Mol. Microbiol., 1994, 14(4):691-703. This ground for rejection is respectfully traversed and reconsideration is requested for the following reasons.

The method of applicants' invention comprises bringing the sample into contact with an *H. pylori* bacterial strain, or an extract thereof, having an aflagellate phenotype resulting from a mutation in the *flbA* gene such that either the *flbA* gene is no longer expressed in the *H. pylori* bacterial strain, or the expression of the *flbA* gene in the *H. pylori* bacterial strain does not enable the A and B flagellins or the sheath that contains them to be biosynthesized and, if this is the case does not enable the *H. pylori* anchoring protein or the hook to be synthesized.

The O'Toole et al. reference clearly shows that the mutants described therein make FlaA and FlaB proteins. This is very different from applicants' mutant, which

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make neither protein. This is evident from the following teachings in applicants' specification:

> The invention is also directed towards bacterial strains of helicobacter pylori which possess an aflagellate phenotype, which phenotype results from the mutation, by substitution, addition and/or deletion of bases or of a nucleotide fragment, of the above-defined nucleotide sequence of the flbA gene involved in the regulation of the biosynthesis of the flagellar proteins of H. pylori.
>
> This modification of the flbA gene makes it possible to obtain a strain of the aflagellate type, that is [sic] which no longer expresses the FlaA and FlaB proteins and which preferably no longer expresses the proteins of the sheath.

(Page 7, lines 3-15).

The rejection under 35 U.S.C. §102(b) should be withdrawn because the O'Toole et al. reference does not disclose all of the features of applicants' claims.

Finally, claims 40-41 were rejected under 35 U.S.C. §103(a) as being unpatentable over either Haas et al. or O'Toole et al. in view of Lelwala-Guruge et al., Scan. J. of Infect. Dis., 1992, 24(4):457-65. The Haas et al. and O'Toole et al. references were applied as above, and the Lelwala-Guruge et al. reference was cited for its alleged teachings of extraction of *H. pylori* proteins with acidic glycine buffer, and for the preparation of antigens for immunological detection via an ELISA. According to the Office, it would have been *prima facie* obvious to one of skill in the art at the time the invention was made to combine the teachings of these three references. This rejection is respectfully traversed.

As previously noted, neither the Haas et al. nor the O'Toole et al. references describe a method for the *in vitro* detection of an infection due to *H. pylori* in a sample of biological fluid from a patient, wherein the method comprises bringing the sample into

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contact with an *H. pylori* bacterial strain, or an extract thereof, having an aflagellate phenotype resulting from a mutation in the *flbA* gene such that either the *flbA* gene is no longer expressed in the *H. pylori* bacterial strain, or the expression of the *flbA* gene in the *H. pylori* bacterial strain does not enable the A and B flagellins or the sheath that contains them to be biosynthesized and, if this is the case does not enable the *H. pylori* anchoring protein or the hook to be synthesized. As the Office recognizes, the Lelwala-Guruge et al. reference does not remedy these deficiencies. None of the references, either alone or in combination, disclose all of the features of applicants' invention, and accordingly, the rejection under 35 U.S.C. §103(a) cannot stand.

In conclusion, applicants respectfully submit that this application is now in condition for allowance. Favorable action at the Examiner's early convenience is courteously solicited.

Please grant any extensions of time required to enter this response and charge any additional required fees to our deposit account 06-0916.

Respectfully submitted,

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